UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/002,653	10/19/2001	Ralph-Heiko Mattern	INT-0004	2405

7590 12/28/2004

Licata & Tyrrell P.C.
66 E. Main Street
Marlton, NJ 08053

EXAMINER	
NAFF, DAVID M	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 12/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/002,653	MATTERN ET AL.	
	Examiner	Art Unit	
	David M. Naff	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 October 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-9 and 11-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-9 and 11-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

An amendment of 10/7/04 amended the specification, amended claims 5 and 13, and added new claims 14-16. A declaration by Donald Nociolo was submitted with the amendment.

Claims examined on the merits are 2-9 and 11-16, which are all claims in the application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 2-9 and 11-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yannas et al (4,060,081) or Yannas et al (4,280,954) in view of Li (5,674,290) for reasons in the previous office action of 4/7/04 and for reasons herein.

The claims are drawn to a scaffold or matrix and method for producing and using the scaffold or matrix wherein the scaffold or matrix comprises a collagen and glycosaminoglycan co-precipitate cross-linked with glutaraldehyde at a density of cross-linkages and under conditions which stabilize the scaffold or matrix toward electron beam radiation at about 15 to about 80 kGy so that the scaffold or matrix retains characteristics to function as a structural support for cell and tissue growth. In some claims, the scaffold or matrix is terminally sterilized with electron beam radiation. New claims 14 and 15 require the conditions to comprise glutaraldehyde in an acetic acid solution, and new claim 16 requires a gluraraldehyde concentration of 0.5%.

Yannas et al ('081) disclose producing a composition containing a collagen and glycosaminoglycan co-precipitate cross-linked with glutaraldehyde (cols 15 and 16), and which can be sterilized with irradiation (col 12, line 52). The composition can be used as artificial graft to replace the function of normal skin and provide a template for cellular regeneration (col 14, lines 48-50). A silicone polymer layer may be present (col 13, line 29).

Yannas et al ('954) disclose producing an implant containing a collagen and glycosaminoglycan co-precipitate cross-linked with glutaraldehyde similar to Yannas et al ('081). The cross-linked co-precipitate may be sterilized (col 23, lines 19-37).

Li discloses preparing an implant (col 6, lines 10-24) by co-precipitating collagen and glycosaminoglycan, cross-linking, packaging, and sterilizing with gamma-irradiation (col 6, lines 22-23). Alternative to gamma-irradiation, electron beams may be used for sterilizing (col 6, lines 48-52 and col 1, lines 28-30).

It would have been obvious to use electron beam radiation to carry out irradiation sterilization of the composition of Yannas et al ('081) or the sterilization of Yannas et al ('954) as suggested by Li disclosing electron beam irradiation as an alternative to gamma irradiation for sterilizing an implant made of a cross-linked co-precipitate of collagen and glycosaminoglycan. Li discloses a gamma irradiation dosage of 15 to 35 kGy, and it would have been obvious to employ a similar dosage when using electron beam irradiation. Cross-linking conditions disclosed by Yannas et al ('081) or ('954) will

inherently provide a cross-linkage density as claimed to stabilize for electron beam radiation. Moreover, it would have been obvious to provide a cross-linkage density for desired stability since Yannas et al ('081) disclose that degree of solubility and resistance to resorption can be controlled by the degree of cross-linking (col 9, lines 25-40), and Yannas et al ('954) disclose cross-linking to a desired density (col 8, lines 50-55). Additionally, when using electron beam radiation for sterilization as suggested by Li et al, it would have been obvious to use cross-linking conditions that provide a suitable stability since Yannas et al intend to produce a stable cross-linked collagen-GAG matrix. The conditions of dependent claims would have been obvious from conditions disclosed by the references. Yannas et al ('081) and ('954) disclose a silicone layer as in claim 2, and Li discloses packaging prior to irradiation as in claim 9. The percent glutaraldehyde in claims 6 and 8 is not unobviously different the concentration of glutaraldehyde used by Yannas et al ('081) and ('954). As to new claims 14 and 15, Yannas et al disclose citric acid, and acetic acid would have been an obvious alternative since it would have been apparent that the acids are similar in view of Yannas et al using either acid for dispersing collagen ('081, col 15, line 7), and using acetic acid to produce a collgen and glycosaminoglycan co-precipitate ('081, col 15, line 50). As to new claim 16, Yannas et al ('081) (col 18, lines 1-10) and Yannas et al ('954) (col 15, lines 40-50) use two steps of cross-linking in 0.025 M glutaraldehyde.

Using 0.5% glutaraldehye would have been an obvious alternative to cross-linking twice with 0.025 M glutaraldehye.

Response to Arguments

Applicants urge that the matrices of Li et al do not disclose GAG. However, applicants apparently over looked Example 3 of Li et al which is directed to making collagen implants containing glycosaminoglycan.

The Nociolo Declaration asserts that gamma radiation did not provide satisfactory results for the particular collagen-GAG matrix being sterilized. However, Li et al suggest electron beam irradiation as an alternative to gamma irradiation. Therefore, if one considers gamma irradiation to be unsuitable, it would have been obvious to use electron beam irradiation suggested by Li et al as an alternative. While there are differences in gamma and electron beam irradiation, these differences would have been apparent to one of ordinary skill in the art, and to select one over the other because its known properties are considered to be preferred would have been obvious.

Applicants urge that glutaraldehyde cross-linking is dependent on conditions other than concentration such as pH, buffering agent, etc. However, the claims do not require a pH and buffering agent unobviously different than used by Yannas et al that has been established by evidence to provide a cross-linkage density different than obtained by Yannas et al. Yannas et al is not silent about pH as urged by applicants, since in col 18, line 7, a pH of 7.4 is used. It is granted that Yannas et al use citric acid. However, it has not

been established that acetic acid is critical to the present cross-linking and that citric acid cannot be used. Due to Yannas et al using cross-linking conditions similar to those disclosed in present specification, it appears Yannas et al obtain a cross-linking density as required by the present claims. Furthermore, Yannas et al suggest that the degree of cross-linking can vary to provide a preferred degree of solubility and resistance to resorption. When using electron beam irradiation to sterilize as suggested by Li et al, one is obviously going to cross-link to a density to obtain a stable matrix after irradiation, or otherwise the matrix will be unsuitable for use.

Claim Rejections - 35 USC § 102

Claims 2-8 and 12-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Yannas et al (4,060,081) or (4,280,954) for reasons in the previous office action and for reasons herein.

The invention and references are described above.

The cross-linked collagen/glycosaminoglycan matrix of Yannas et al is inherently cross-linked sufficiently to retain characteristics after sterilizing as required by the claims. The matrices of Yannas et al can be sterilized, and it does not appear using electron beam radiation will produce a matrix differing substantially in chemical and physical properties.

Response to Arguments

Applicants refer to conditions disclosed in the present specification as being different than used by Yannas et al. However,

there is inadequate evidence to establish that specific conditions in the present specification produce a cross-linked collagen-GAG matrix that is materially different from that obtained by Yannas et al. As noted above, the use of acetic acid is an obvious alternative to citric acid, and it has not been established that citric acid will not work in the present invention. Additionally, as noted above, Yannas et al disclose a pH of 7.4. It has not been established by evidence that this pH will not be workable in the present invention, and the claims do not require a substantially and unexpectedly different pH.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David M. Naff

whose telephone number is 571-272-0920. The examiner can normally be reached on Monday-Friday 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David M. Naff
Primary Examiner
Art Unit 1651

DMN
12/23/04